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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,495	12/05/2003	Richard B. Borgens	3220-73828	2575

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EXAMINER	
MORRIS, PATRICIA L	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 10/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,495	BORGENS ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4 and 15-17 are under consideration in this application.

Election/Restrictions

Applicant's election without traverse of Group I and compound 2 in the reply filed on August 9, 2004 is acknowledged.

This application has been examined with regard to the elected compounds wherein R^2 represents $-COR^3$, R^3 is OR wherein R is a C_1-C_{20} alkyl group, R^6 represents H, alkyl, NO_2, F, Cl, Br and I and R^1, R^7-R^9 as set forth in claim 1, exclusively.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 and 15-17 are rejected under 35 U.S.C. 102(a), (b) and/or (e) as being anticipated by Czekaj et al. (US 2003/0092698), Tulshian et al. (US 6,727,254), Pauls et al. (US 2002/0045613), Altenburger et al. (US 6,680,329), Ewing et al. (WO 01/07436), Bastian et al. (US 6,265,416), Chen et al. (US 5,990,109), Doll et al. (US 5,880,128), Tanga et al. (CA 127: 161747), Takefuji et al. (US 5,763,463), Konishi et al. (JP 3-

181462), Shimizu et al. (CA 112:193716), Matondo et al. (J. Agric. Food Chem. 1990, 38, 1106-1109), Kirazis et al. (CA 112:138873), Sakamoto et al. (CA 108:75166), Von Bebenburg et al. (CA 93:95098), Bickel et al.(US 3,929,779), Pews et al. (US 3,804,844), Yakhontov et al. (CA 69 :86786), Imperial Chemical (CA 68:59438), Clark-Lewis et al. (CA 57:23142) and Takahashi et al. (CA 51 :12837).

Czekaj et al. specifically disclose 3-iodo-4-pyridinyl, 1,1-dimethylethyl ester carbamic acid. Note example 9 [0201] therein.

Tulshian et al. recite the instant compound wherein R^7 is Br, R^6, R^8 and R^9 are hydrogen and R^3 is tert-butoxy. Note example 18, column 16, line 55, therein.

Pauls et al. disclose the instant compounds wherein R^7 is chlorine and R^6 is either hydrogen or methyl. Note example 4 [0385] and [0387] therein.

Altenburger et al. specifically disclose 3,5-dibromo-4-pyridinyl-1,1-dimethylethyl ester carbamic acid. Note example 8 therein.

Ewing et al. disclose the instant compounds wherein the pyridine ring is substituted with chlorine or chlorine and iodine. Note example 247 A and B therein.

Bastian et al. disclose 3-methyl-4-pyridinyl)-1,1,-dimethylethyl ester carbamic acid. Note example 3, column 21, lines 33-34, therein.

Chen et al. specifically recite the instant compound wherein R^7 represents chloro, R^8 represents nitro and R^3 is tert-butoxy.

Doll et al. and Clark-Lewis et al. specifically disclose the compound of claim 15 herein. Note preparative example 2 of Doll et al.

Tanga et al. disclose the instant compounds wherein the pyridine is substituted with methyl and R^3 is methoxy. Note RN 193690-59-4, 193690-66-3, etc.

Takefuji et al. recite 3-chloro-2-ethyl-4-pyridinyl-,methyl ester carbamic acid. Note preparation example 4 therein.

Konishi et al. disclose the many of the instant compounds wherein R is alkyl. Note the tables of compounds recited on pages 4-5 therein.

Shimizu et al. specifically disclose 2-chloro-4-pyridinyl-,propyl ester carbamic acid. Note RN 121433-24-7.

Matondo et al. disclose the claimed methyl and dodecyl N-(4-pyridyl)carbamates.

Kiriazis et al. disclose the instant compound wherein R^1 is methyl and R is propyl. Note RN 125867-16-5.

Sakamoto et al. recite 3-bromo-4-pyridinyl-ethyl ester carbamic acid. Note RN 112671-56-4.

Von Bebenburg et al. specifically recite 2,6-dichloro-4-pyridinyl-ethyl ester carbamic acid. Note RN 73895-95-1.

Bickel et al. disclose the claimed compound wherein R is 1,1-dimethylpropyl. Note column 15, lines 31-32 therein.

Pews et al. and Imperial Chemical disclose the instant compounds wherein R is methyl, ethyl or propyl and R^6-R^9 represent chlorine, fluorine or methyl. Note examples 3 and 4 of Pews et al. therein.

Yakhontov et al. specifically disclose 4-pyridinecarbamic acid, 3-ethyl ester, monohydrochloride. Note RN 19984-03-3.

Clark-Lewis and Takashi et al. teach the instant nitro substituted pyridines. Note RN 98279-90-4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1- 4 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Czekaj et al., Tulshian et al., Pauls et al., Altenburger et al., Ewing et al., Bastian et al., Chen et al., Doll et al., Tanga et al., Takefuji et al., Konishi et al., Shimizu et al., Matondo et al., Kirazis et al., Sakamoto et al., Von Bebenburg et al., Bickel et al., Pews et al., Yakhontov et al., Imperial Chemical, Clark-Lewis et al. and Takahashi et al.

As discussed supra, the references generically embrace the instant compounds.

It is believed that one having ordinary skill in the art would have found the claimed compounds prima facie obvious, since they are generically embraced by the disclosed formula; In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). See also In re Malagari, 499 F.2 1297, 182 USPQ 549 (CCPA 1974); In re Lemin, 332 F.2d 839, 141 USPQ 814 (CCPA 1964); In re Rosicky, 276 F.2d 656, 125 USPQ 341 (CCPA 1960). The requisite motivation for arriving at the claimed compounds stems from the fact that they fall within the generic class of compounds disclosed by the references. Accordingly, one having ordinary skill in the art would have been motivated to prepare any of the compounds embraced by the disclosed generic formula, including those encompassed by the claims.

It is believed well settled that a reference may be relied upon for all that it would have reasonably conveyed to one having ordinary skill in the art. In re Fracalossi, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); In re Lamberti, 545 F.2d 747, 192 USPQ 278 (CCPA 1976); In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976); In re Susi, supra.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The expression solvate and polymorph are employed in claims 1-4 with no indication given as to what the solvates really are. It is well known that that solvents can affect chemical stability of the compounds.

One should be able, from a reading of the claims, determine what that claim does or does not encompass.

Why? Because that claim precludes others from making, using, or selling that compound for 20 years. Therefore, one must know what compound is being claimed.

The unknown solvates are so broad that they cause the claim to have a potential scope of protection beyond that which is justified by the specification disclosure.

The written description is considered inadequate here in the specification. Conception of the intended solvates and polymorphs should not be the role of the reader. Applicants should, in return for a 20 year monopoly, be disclosing to the public that which they know as an actual demonstrated fact. The disclosure should not be merely an invitation to experiment. This is a 35 USC 112, first paragraph. If you (the public) find that it works, I claim it, is not a proper basis of patentability. In re Kirk, 153 USPQ 48, at page 53.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is a lack of description as to whether the pharmaceutical carriers are able to maintain the compound in the polymorphic form or solvates claimed. Desolvation may occur. Processing a compound into a pharmaceutical composition could desolvate or create a different polymorph than the polymorphs being claims or even back to the compound itself.

The specification fails to describe the compounds and pharmaceutical compositions claimed in terms of their X-ray diffraction pattern or infrared spectrum data.

There is also no description as to how applicants produced and isolated the particular solvates and polymorphs being claimed. Only when solvent is incorporated into the crystal lattice of the compound in stoichiometric proportions, are particular solvates formed. Applicants would have to show how the particular solvates and polymorphs in the claims are isolated.

Chemical & Engineering News discloses that formulation of drugs or pharmaceuticals in its metastable forms, for example, one polymorph, is highly unpredictable. The metastable forms will disappear and change into the most thermodynamically stable form. The specification lacks description of how the polymorphs and pharmaceutical compositions can be prepared in order to maintain the particular compound of a particular form with the particular infrared spectra and X-ray diffraction being claimed. Disclosure of X-ray diffraction patterns for the polymorphs and pharmaceutical compositions comprising the polymorphic forms are lacking in the specification. The specification has also not described how the polymorph forms and

compositions being claimed will be maintained and prevented from converting to other forms when used in the treatment of injured nerve tissue.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of novel polymorphic and solvate forms of the instant salt and compositions.

State of the Prior Art

Polymorphs arise when molecules of a compound stack in the solid state in distinct ways. (See Chemical Engineering News, page 32). Although identical in chemical composition, polymorphs can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. Additionally, solids

may form solvates. Polymorphs tend to convert from less stable to more stable forms. (See Chemical Engineering News, page 32). No method exists to predict the polymorphs of a solid compound with any significant certainty. In drug design, it is best work with the most stable polymorph, because it will not covert any further, however, the most stable polymorph usually is the least soluble. To improve bioavailability, drug companies sometimes trade off polymorph stability with solubility, choosing to work instead with the less stable forms first, also known as the metastable forms. Polymorphs can convert from one form to another during the manufacturing process of a pharmaceutical drug. See Chemical Engineering News. Page 33, which will changed the pharmacological affects of the drug. This is why it is important to monitor the polymorph during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

The specification fails to disclose the X-ray diffraction pattern and infrared spectra of compounds of particular polymorphs and the compositions containing a particular polymorph.. Polymorphs often change into other polymorphs during drug manufacture (See Chemical Engineering News) in a pharmaceutical composition

The breadth of the claims

The breadth of the claims are drawn to the unknown solvates and polymorph forms in addition to the pharmaceutical compositions.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the polymorphs and solvates and their pharmaceuticals compositions being claimed and

verifying that they have the specific X-ray diffraction patterns being claimed which are not disclosed in the specification.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 provides for the use of treating injured mammalian nerve tissue but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 3 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The plural 's' on salts makes claim 4 read on mixtures rather than specfic compounds.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, "Claims measure invention and resolution of invention must be based on what is claimed".

The C.C.P.A. in 1978 held a that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim": In re Priest, 199 USPQ 11, at 15.

Drawings

The formal drawings filed on December 5, 2003 have been accepted.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
September 30, 2004